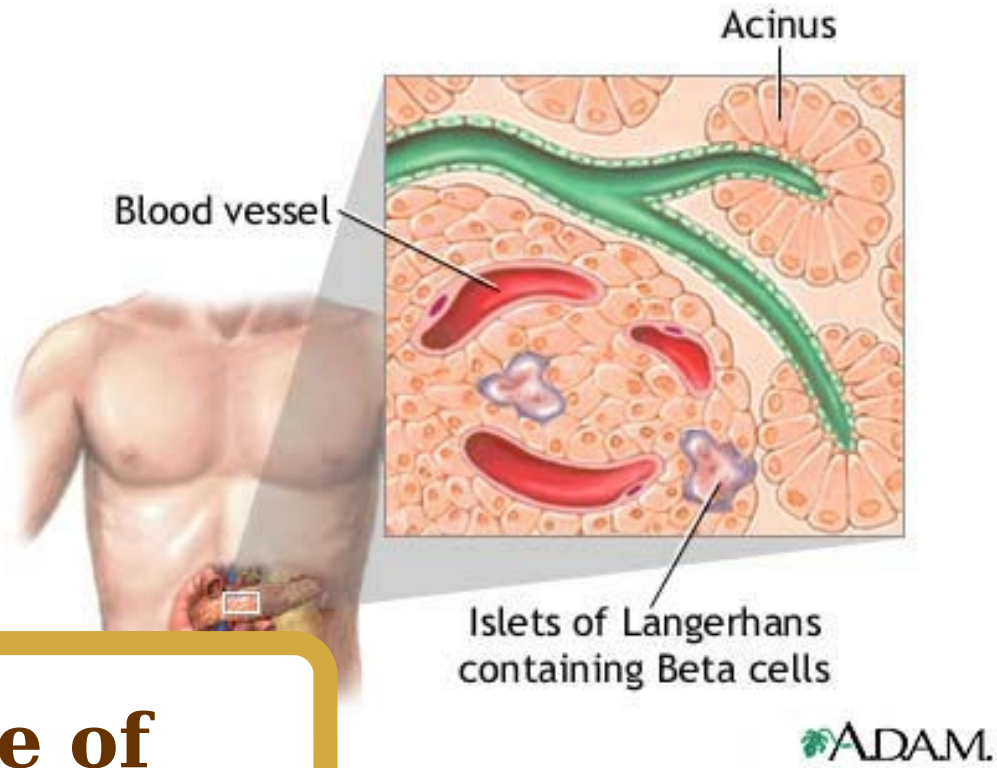


Armed Forces College of Medicine

AFCM

Diabetes Mellitus

Dr Maggie Maher

INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1- Interpret metabolic changes of type 1 DM

2- Interpret metabolic changes of type 2 DM

3- Demonstrate diagnostic parameters of DM

4- Describe biochemical basis of diabetic complications

Case

- Amal a 57 year old woman, weight 110 Kg suffered from Diabetes Mellitus since 15 years. Amal was on oral hypoglycemic medications, until two years ago her medication was changed to injectable insulin. On follow up the doctor ordered for renal function tests and HgA1C for her.

Lab investigations were:

- **Random Bl. Glucose : 310 mg %**
- **HbA1C: 7 % (Normal: 4.5 – 5.7 %)**
- **Creatinine : 1.6 Normal (0.8 – 1.2 mg /dl)**
- **Urea: 46 mg/dl (20 – 40 mg/dl)**

Diabetes Mellitus

Diabetes is not one disease, but rather is a heterogeneous group of syndromes characterized by an elevation of fasting blood glucose caused by a relative or absolute deficiency in insulin.

Disturbance in carbohydrate, lipid, protein and mineral metabolism.

Metabolic changes in Type 1 diabetes.

1-Carbohydrates metabolism:

- The hallmarks of diabetes mellitus.

Hyperglycemia

is caused by

↓glucose uptake by GLUT4.

muscle and

Increased hepatic production of glucose (glycogenolysis and

2- Lipid metabolism

(*Hypertriacylglycerolemia*)

- i). ↑Lipolysis → ↑Release of free fatty acids

ii) Also ↑ synthesis (re-esterification) of TAG → VLDL → in the liver

Hypertriacylglyc-erolemia

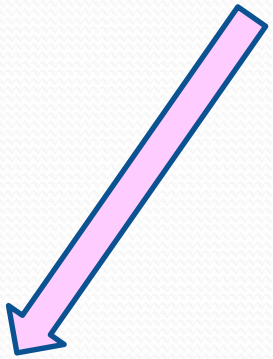
Because lipoprotein degradation catalyzed by *lipoprotein lipase* in the capillary beds of muscle and adipose tissue is low in diabetics

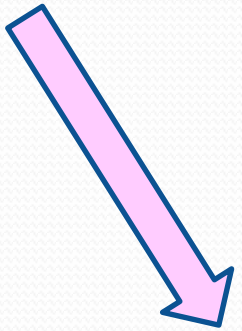
(synthesis of the enzyme is decreased when insulin levels

are low)

SO the plasma chylomicron and VLDL levels are elevated, resulting in hypertriacylglycerolemia

III- Ketoacidosis (Ketosis)





Increased lipolysis and mobilization of FA from adipose tissues

Accelerated β-oxid. & Ketone Bodies formation

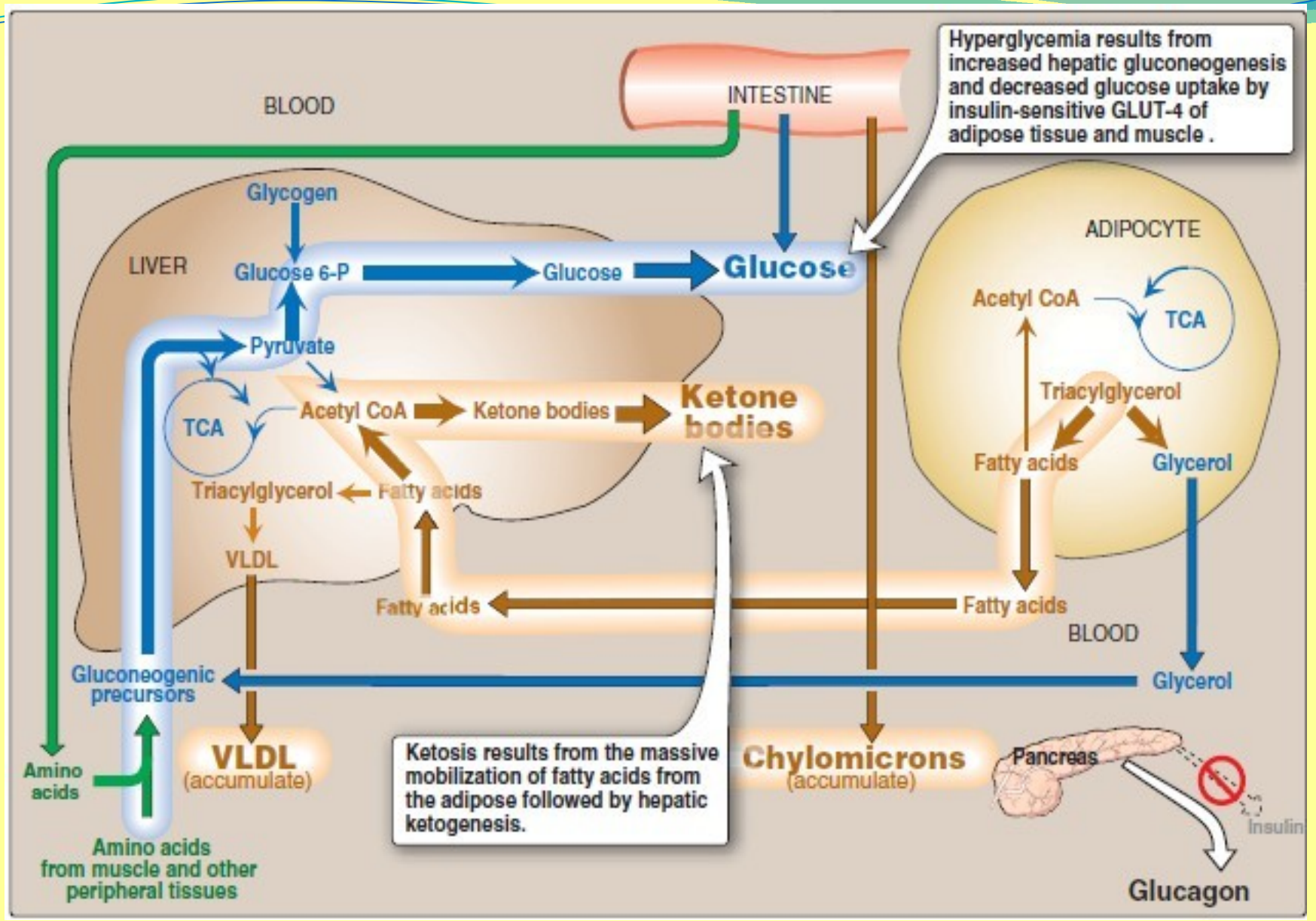
3. Protein metabolism

↑ protein breakdown

- **Gluconeogenesis**

Decrease antibody formation

- **Recurrent infection**



Lippincott's Illustrated Reviews- 6th edition.

Metabolic changes in Type 2 diabetes.

These are mainly the result of insulin resistance expressed primarily in **liver, muscle and adipose tissue.**

1. **Hyperglycaemia:**
   caused by **diminished** peripheral utilization (due to defective uptake by GLUT4)

2- Lipid metabolism

(*Hypertriacylglycerolemia*)

- i). ↑Lipolysis → ↑Release of free fatty acids

ii) Also ↑ synthesis (re-esterification) of TAG in the liver → VLDL → ***Hypertriacylglycerolemia***

Because lipoprotein degradation catalyzed by *lipoprotein lipase* in the capillary beds of muscle and adipose tissue is low in diabetics

(synthesis of the enzyme is decreased when insulin levels

are low)

SO the plasma chylomicron and VLDL levels are elevated, resulting in hypertriacylglycerolemia

NB: Ketosis is minimal because insulin is present which decreases hepatic ketogenesis.

Diagnosis of diabetes mellitus.

1- The onset of Type 1 diabetes is typically during childhood and symptoms develop rapidly.

2- **Patients with Type 1 diabetes can usually be recognized by the abrupt appearance of:**

polyuria (frequent urination),
polydepsia (excessive thirst),
polyphagia (excessive hunger),

3- These symptoms are usually accompanied by fatigue, weight loss, and weakness.

Diabetes Diagnosis

Stage	Test	
	Fasting Plasma Glucose (FPG)	2- Hour Oral Glucose Tolerance Test
Diabetes	≥126 mg/dl	≥200 mg/dl
Pre-diabetes	≥100 and <126 mg/dl	≥140 and <200 mg/dl
Normal	<100 mg/dl	<140 mg/dl

Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 2004;27 S5-S10.
Glucose Tolerance Test; accessed August 6, 2008 at http://en.wikipedia.org/wiki/Glucose_tolerance_test.

Glycosylated hemoglobin

Glycosylated hemoglobin is non-enzymatic conjugation of Hg with glucose.

HbA1C is the investigation of choice to monitor therapy as it gives an idea about the

Chronic effects of Diabetes (type I & II):

1- Sorbitol pathway:

Aldose Reductase

Glucose → sorbitol

↓

smotic damage to the cells

Cataract

Note: Insulin is not required for the entry of glucose into cells of the lens, **retina**, liver, kidney, red blood cells and in cells of the ovary and seminal vesicles.

-In these cells , increased intracellular glucose and
its metabolites e.g**. sorbitol** in the lens causes cataract.

2-Abnormal glycation of proteins:

Non enzymatic
(HB, collagen of the glomerular basement membrane, proteins of small blood vessels and proteins of the nervous system)

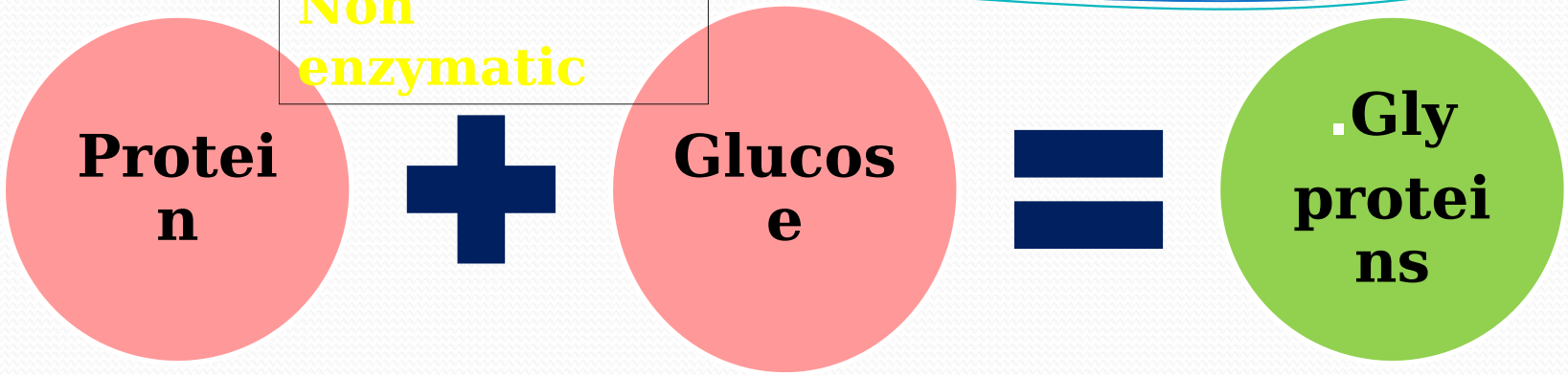
Mediating early microvascular changes.

The end products of glycation are termed **AGEs** (Advanced glycation end products).

They bind to specific receptors on

Endothelial cells and macrophages

Non enzymatic



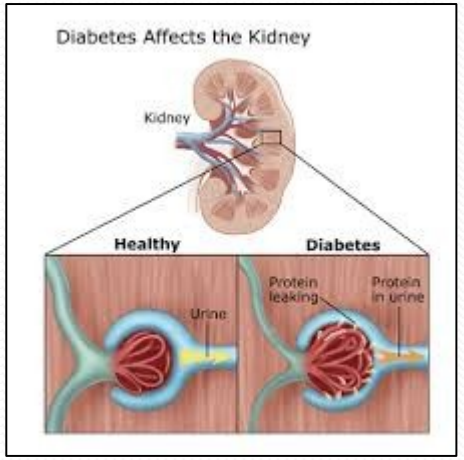
Advanced glycated end products (AGEs)

They bind to specific receptors on endothelial cells and macrophages

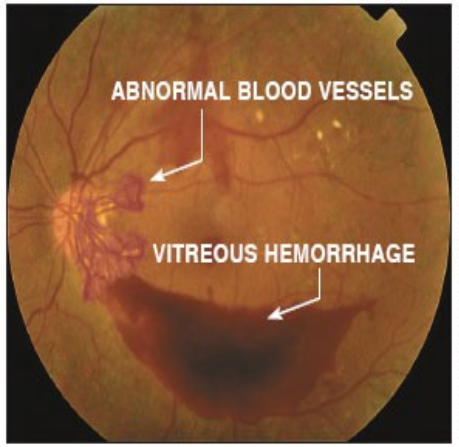
ANGIOPATH

Angiopathy

- Affects small blood vessels as capillaries especially those of the kidneys and retina of the eye.



Diabetic Nephropathy



Diabetic Retinoopathy

The long-standing elevation of blood glucose causes
The chronic complications of diabetes which are:

- **atherosclerosis (include CVD disease)**

-retinopathy
-nephropathy
-neuropathy

Control of blood glucose improves by ttt and HbA_{1C} level decreases .

	Type 1 Diabetes	Type 2 Diabetes
AGE OF ONSET	Usually during childhood or puberty; symptoms develop rapidly	Frequently after age 35; symptoms develop gradually
NUTRITIONAL STATUS AT TIME OF DISEASE ONSET	Frequently undernourished	Obesity usually present
PREVALENCE	900,000 = 10% of diagnosed diabetics	10 Million = 90% of diagnosed diabetics
GENETIC PREDISPOSITION	Moderate	Very strong
DEFECT OR DEFICIENCY	β Cells are destroyed, eliminating production of insulin	Insulin resistance combined with inability of β cells to produce appropriate quantities of insulin
FREQUENCY OF KETOSIS	Common	Rare
PLASMA INSULIN	Low to absent	High early in disease; low in disease of long duration
ACUTE COMPLICATIONS	Ketoacidosis	Hyperosmolar state
TREATMENT WITH ORAL HYPOGLYCEMIC DRUGS	Unresponsive	Responsive
TREATMENT	Insulin is always necessary	Diet, exercise, oral hypoglycemic drugs; insulin may or may not be necessary

Lecture Quiz

Which one of the following lab investigations is done to follow up a diabetic case during last 3 months?

A. Fasting blood sugar

B. Post prandial blood sugar

C. Glycated hemoglobin

D. OGTT

E. Random blood sugar.

SUGGESTED TEXTBOOKS

- Lippincott’s Illustrated Reviews- 6th edition.
- Harper’s Illustrated Biochemistry-29th edition.


Thank you!